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THE HISTORY AND CONTROL OF YELLOW FEVER

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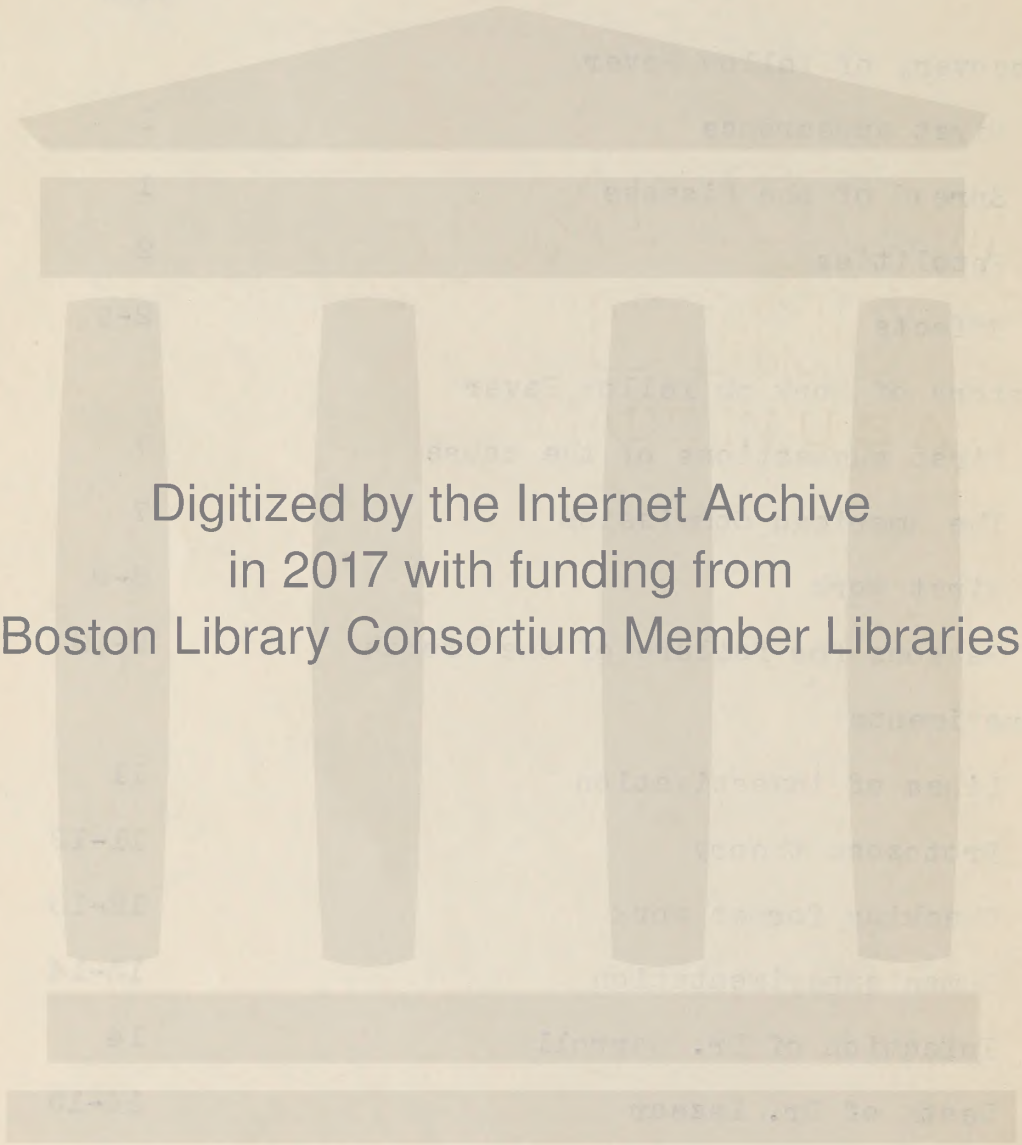

THE HISTORY AND CONTROL OF YELLOW FEVER

Discovery of Yellow Fever

Yellow fever is one of the most virulent of human diseases. So far as we know, it first appeared in Central America over three hundred years ago. In 1750, it crossed from there into Cuba, then across the Gulf of Mexico into Charleston, Mobile, New Orleans, and Galveston. Even the more northern cities of Baltimore, Philadelphia, New York, and Boston did not escape its havoc. In two hundred and eight years it invaded the United States ninety-five times, and since 1793 there have been not fewer than one hundred thousand deaths due to it in this country alone. (1) (Fig.1)

The northern cities were able, by rigid quarantine measures, to prevent serious epidemics after the early part of the nineteenth century, but from the West Indies and Central America the disease was occasionally introduced and prevailed from time to time epidemically in the Southern States. In 1853, it raged throughout this region, New Orleans alone having a mortality of 8,000. The last widespread epidemic occurred in 1878, chiefly in Louisiana, Alabama, and Mississippi, but spreading up

(1) Peabody, J. E. -- The Conquest of Yellow Fever -- pages 1,2

the Mississippi Valley as far as Cairo, Illinois, and attacking Memphis, Tennessee. In this year there were 125,000 cases and 12,000 deaths. In 1882, there were 192 deaths at Pensacola; in 1887, 62 deaths in the Southern States: in 1893, 52; in 1897, 484 deaths; in 1898, 2,456 cases with 117 deaths; in 1903, 139 deaths were recorded, mostly at Laredo, Texas; and in 1905 there was a serious outbreak in New Orleans and in neighboring towns, including one locality in Mississippi in which 911 deaths were recorded.

The actual loss of life from yellow fever during all those years, when compared with the loss from other diseases was comparatively slight, but the death-rate was perhaps the most insignificant feature of the devastation which yellow fever epidemics produced, and the disease itself was only a small part of the trouble which it brought to the Southern States. When the disease was once discovered in epidemic form the whole country became alarmed; commerce in the affected region was brought almost to standstill; many cities were largely deserted; people died from exposure while camping out in the higher lands; rigid quarantines were established and innocent persons were shot while trying to pass the quarantine lines; nearly all industry ceased

for the time.

The commerce of the South during the epidemic of 1878, for example, fell off 90 per cent. The hardships of the people cannot be estimated in monetary terms. With such industrial and commercial conditions existing from Texas to South Carolina, many industries of the North suffered; indeed, the effect of a yellow-fever summer in the South was felt not only all over the United States, but in many other portions of the world. All these conditions, however, do not sum up the total loss to the national prosperity. Cities like Galveston, New Orleans, Mobile, Memphis, Jacksonville, and Charleston, subject to occasional epidemics, did not prosper as they should have done. Their progress was seriously impeded by this one cause, and thus the industrial development of the whole South was greatly retarded. (1)

"In the terrible epidemic of 1793 in Philadelphia," says Miss Hallock in her account of the life of Walter Reed, "all the streets and roads leading from the city were crowded with families flying to the country for safety. So many doctors were sick or had died of yellow fever that 'at one time there were only three physicians who were able to visit patients, and at this time there

(1) Howard, L. O. -- The Insect Menace -- pages 173, 174

were probably not fewer than 6,000 persons ill with the fever.' Dr. Rush, then a physician in Philadelphia, related that a cheerful countenance was scarcely to be seen in the city for six weeks. Once on entering the house of a poor man, he met a child of 2 years who smiled in his face, and he says, 'I was strangely affected by this sight.' Few persons were met in the streets except those who in quest of a physician, a nurse, or the men who buried the dead. The hearse alone kept up the remembrance of the noise of carriages or carts in the street."

Previous to the yellow fever epidemic of 1878, in the City of Memphis, Tennessee, the City had already suffered seriously from war, reconstruction, cholera, small-pox, and two previous epidemics of yellow fever (in 1867 and in 1873) and in the latter year over 2000 of the inhabitants had died. By the middle of August, 1878, it had become generally known that the dread disease had again reached the city. "Business stopped", says the official report of the epidemic, "stores and offices were hastily closed. Men, women, and children poured out of the city by every avenue of escape... To the cities of the far north and the far west they fled, too many of them to die on the way like dogs, neglected

and shunned as if cursed by God.

"On the 14th of September, the day of the heaviest mortality, many buoyant natures succumbed. They looked about them for convalescents, but they were not to be found: a few of them were reported, but they seemed nearly all of them to have been permanently disabled. The cry for food, for clothing, for money, for doctors, for as many as a thousand coffins, went out by telegraph to the ends of the earth, and a prompt and a generous response came back. The medical estimate puts the total population, during the epidemic, at 19,000, and the total sick at 17,600, the deaths being 5,150, a little less than one-third." (1)

As one scourge followed another, the doctors and government agencies did their utmost to find the cause and to check the ravages of "yellow jack." Desperate measures of quarantine were instituted and property of great value was destroyed in these vain attempts. Up to 1793 this disease was generally believed by people at large to be "a visitation of God," and all that could be hoped for was that the frosts, which always stayed its progress, would come early. In the treatment of yellow fever by the medical men, however, almost every known measure under the sun had been tried, at various times,

(1) Peabody, J. E.--The Conquest of Yellow Fever--page 3 (from: J. M. Keating, "A History of the Yellow Fever Epidemic of 1878.")

but with little success. Even rattlesnake poison was employed in Cuba, and some asserted it was more or less effective. The practice of magic was also employed, but to no avail.

It would be impossible to place the total money loss to be laid at the door of the yellow-fever mosquito at a tremendous sum with any danger of exaggeration. The last century drew to a close with the tropics still visited by the dread epidemics. But all this is past, and in all probability another epidemic will never occur in the United States. Yellow fever has probably been wiped out, and there exist to-day, so far as the reports of the Public Health Service indicate, only perhaps half a dozen cases, in West Africa and Brazil.

The statistics and computations may appear a bit burdensome, but they serve to bring vividly to mind the awful visitations and effects of the disease. Let us turn to the history of yellow fever from a different point of view --- in order that we may more fully understand all the circumstances surrounding it, feeling secure in the knowledge that, interesting as it is, we may view it as "a matter of historical interest." (1)

(1) Plath, O. E. -- Class Lecture, "Applied Entomology" March 27, 1934

History of Work on Yellow Fever

It was in 1848 that Dr. Josiah Nott, of Mobile, suggested that mosquitoes might be responsible for or connected with the spread of yellow fever. Unfortunately, the subject was not even regarded with any great amount of seriousness and the suggestion was soon forgotten. In 1881, however, Dr. Carlos Finlay, of Havana, expressed the belief that yellow fever was propagated by the mosquito, the infecting agent being transferred on the proboscis of the insect. Once again the suggestion was doomed to failure. It had, as presented, very little scientific substantiation and was consequently disregarded -- although from time to time it was forwarded as a highly probable theory, compatible with the facts -- until nineteen years later when a commission from the United States Army, headed by Major Walter Reed, undertook the task of seeking the true factors concerning the disease.

Working with Major Reed in the conquest of the disease were Major James Carroll, Dr. Jesse W. Lazear and Dr. Aristides Agramonte. These four men were embarked upon the investigation which was to win them

the undying gratitude of nations all over the world.

There were recognized, prior to the work of the committee, striking resemblances between malaria and yellow fever. They both occur in low areas and "are commonest in the situations where, and seasons when, mosquitoes are most abundant, disappearing after the severe frosts, which drive the insects into hibernation". (1) Direct inoculation of the blood of a patient will convey either disease. Dr. Calkin, at a meeting of the American Association for the Advancement of Science in New Orleans, stated:

"The asexual protozoan organisms are transferred from the warm blood of birds, or mammals, or man, to the cold environment of the insects' digestive tract. This is accomplished in the case of malaria by mosquitoes belonging to the genus Anopheles."

Because of these facts and the work of Dr. Patrick Manson and Major Ronald Ross of England during the latter part of the last century, it is not surprising that Dr. Reed, soon after his arrival in Cuba, should confer with Dr. Carlos J. Finlay about the task at hand. Added to that, Dr. Henry R. Carter, of the Public Health Service, who for years had served as a quarantine officer, very intelligently passed his observations on to

(1) Mitchell, E. G. -- Mosquito Life -- page 102

Dr. Reed. For many years he (Carter) had observed that when a man developed yellow fever on board ship none of his shipmates became ill, even those who lived in the crowded forecastle with him, until a time considerably in excess of the period of incubation of the disease in man; this led him to believe that yellow fever could not be contracted from the environment of a sick man for a considerable time after he became sick in that environment. In the discussion, Dr. Reed asked Carter, "Are you sure your dates are accurate"? Carter was certain. Then, without any more doubt, Reed declared, "It spells an insect host".

Accordingly, Dr. Reed set to work to test Finlay's and Carter's theory. Dr. Lazear was put in charge of mosquito breeding; Dr. Carroll hunted for possible bacteria that might be the cause of the disease; while Dr. Agramonte studied the bodies of those who had died of yellow fever.

Several factors had been instrumental in the inability of the French doctors, furiously busy to wipe out yellow fever before it itself wiped out every man on the Panama Canal project as well as doctors and scientists in the various stricken areas, to control the spread of the disease. Most importantly, the dissemina-

tion of yellow fever was unknown. This vital point had to be settled scientifically before any effective steps could be taken to eradicate the disease. As a matter of fact, all the steps taken in the prevention and control of the disease previous to the findings of the United States Army Commission, had been exerted in the wrong direction with the result that a great many lives and a tremendous amount of money were spent with no nearing to the mystery of the origin of the disease. For example, it was generally believed that Fomites, filth, and soil conditions were the distributing agencies. Obviously, as we shall see from the experiments to be discussed, such agencies -- though in themselves repulsive to the average person -- are entirely innocent in the essence of the dreaded disease. Now, however, by attacking the problem in the strictly scientific manner in which the Commission set about its work, all guesswork was eliminated, and success became a matter of time.

EXPERIMENTS

Two lines of investigation interested the Commission --- the hunt for the bacterial cause for the disease, and the means by which these "germs" were transmitted from the sick to the new victim. Dr. Reed and Dr. Lazear confined their attention to mosquitoes and mosquito breeding while Dr. Carroll, who had been appointed by his chief to study possible bacteria that might be the cause of the disease, introduced the following arguments for the theory of a protozoan essential in the dissemination of yellow fever. He stated:

It seems quite rational to exclude it from the bacteria, because: (a) It has never been cultivated nor stained by any of our known methods. (b) The work of Marchoux, Salimbeni, and Simond has shown that the blood of a patient after its withdrawal loses its power to infect within two days, if kept exposed to the air, and within five days if air be excluded. (c) The disease has been shown to be absolutely non-contagious in regions where Stegomyia fasciata (calopus) is not present, i.e. in Petropolis, near Rio Janeiro. (d) We know no bacteria that live in the tissues of animals as the

yellow-fever organism does in the mosquito, for months, as a harmless parasite. The logical conclusion, therefore, would seem to be that the parasite of yellow fever belongs to the animal kingdom, because: (a) It is absolutely necessary for its continued existence that it pass alternately through man and the mosquito, and the parasitic existence in those hosts is obligatory. (b) The fact that a period of about two weeks or more must elapse before the contaminated mosquito is capable of infecting, points to a definite cycle of development in that insect. (c) The limitation of its developmental cycle to mosquitoes of a single genus, and to a single vertebrate, conforms to a natural zoological law, and does not agree with our present knowledge of the life history of bacteria. (d) The effects of climate and temperature upon Stegomyia, and upon the rate of development of the yellow-fever parasite within the body of that insect, are exactly the same as the effects of the same conditions upon the Anopheles mosquito and the malarial parasite. (1)

Upon the conceptions of Reed and Carroll were the ensuing experiments based and tried.

The Commission first took up the study of Bacillus icteroides, the organism which Sanarelli, an Italian

(1) Mitchell, E. G. -- Mosquito Life --p.105

physician had declared to be the causative agent in yellow fever. They were unable to isolate this bacillus either from the blood during life or from the blood and organs of cadavers and therefore turned their attention to Finlay's theory of the propagation of yellow fever by means of the mosquito. In this work they had the unselfish and enthusiastic support of Dr. Finlay himself, who not only consulted with them and placed his publications at their disposal but furnished eggs from which their experimental mosquitoes were obtained. This series of experiments nullified for all time any idea that Bacillus icteroides was the cause of the disease. The French Academy of Medicine had already accepted Sanarelli's organism. At the meeting of the American Public Health Association in Indianapolis, Reed, on a post-haste trip to the meeting, routed the advocates of Sanarelli's bacillus in a fiery debate. (1)

In three weeks Dr. Reed was back in Cuba, and work was resumed.

To test the theory of mosquito infection, it was necessary to experiment on human beings, for all attempts to produce yellow fever in guinea pigs, rabbits, monkeys, and other animals had failed. With a display of courage unequaled in the annals of history the members

(1) Major General Robert U. Patterson, Surgeon General -- The Work of Walter Reed and his Associates --

of the Commission subjected themselves to bites by mosquitoes which Dr. Lazear hatched out from eggs furnished by Dr. Finlay. All the members allowed themselves to be bitten and breathlessly awaited the reaction. The result was negative, for no one knew at that time the length of time that must elapse before the yellow fever organism within the mosquito would become capable of causing the disease.

Near the end of August Dr. Lazear showed Dr. Carroll a mosquito he had hatched in the laboratory. This insect had been allowed to bite four yellow fever patients at different intervals. Four days later Dr. Carroll was stricken with the disease, and for three days his life hung in the balance. Fortunately he recovered, and it took six years for the heart of this brave doctor, weakened by the disease to which he had voluntarily exposed himself, to cease beating.

And now we come to the first victim in the conquest of yellow fever.

Dr. Lazear continued his stern experimentations during the illness of Dr. Carroll. While he was collecting blood from a yellow fever patient, a mosquito settled on his hand and he allowed it to take its fill. In a few days he, too, was ill with the disease in its

most deadly form, and within a week died in delirium. His death was an irreparable loss to the Commission.

Dr. Reed, deeply sorry though he was for the illness of Dr. Carroll and almost broken-hearted by the death of Dr. Lazear, felt confident that the long sought solution of the problem had been found. But scientist that he was, he realised that his proof was not certain enough to satisfy a skeptical world which would raise all sorts of objections to his conclusions.

"How do you know," they would say, "that Dr. Carroll and Dr. Lazear had not been infected before the mosquitoes bit them?" "How do you know they had not come in contact with those deadly 'fomites' that are, we are sure, the cause of this disease?" And so this quiet, determined Doctor set himself to devise experiments that would be absolutely convincing. (1)

As the three remaining members of the Commission were discussing the subject that lay uppermost in their minds, John R. Kissinger, a hospital orderly who had served through the Spanish-American War, overheard their plans. He realised that more human beings were necessary for experimental purposes. He enlisted the sympathy and consent of an old friend of his from the same Ohio regiment, John J. Moran. Together they

(1) Peabody, J. E. -- The Conquest of Yellow Fever -- page 10

presented themselves before Dr. Reed and offered themselves as subjects.

Dr. Reed was deeply touched . He realised the danger and almost certain death to which they would be exposed. Surely he must have felt a lump in his throat as they remained fixed in their determination to try to be of service. Dr. Reed then offered them money which they promptly refused.

"We do this," said Kissinger, "solely in the interests of science and the cause of humanity." Thereupon Major Reed touched his cap, saying, "Gentlemen, I salute you."

Thus began an experiment which was to pave the way for the solution of the problem.

About a mile from Quemados, Cuba, in a lonely, uncultivated field an experimental station was established. It was named Camp Lazear in honor of the fellow worker who had given his life a martyr to the cause. The station was open to sun and air, but carefully closed against any possible outside infection. Seven hospital tents were erected, and on November 20 this camp was put under the strictest quarantine. To it came the brave volunteers who were to be experimented upon, and no one but the non-immunes were permitted to enter or leave the

place. These non-immunes were the attendants who went for supplies to the neighboring Columbia Barracks. Every non-immune inmate of the camp was carefully examined three times daily as to temperature and pulse rate, so that every infected individual should at once be removed from the experiment station.

Two weeks of possible danger passed and all the inmates were in healthy condition. Now began the deadly experiments. On December 5, at two o'clock in the afternoon, five promising mosquitoes which had bitten yellow fever patients were permitted to settle down--with Kissinger's free consent--upon him and drank their fill of his blood. Eighty-one hours later, Kissinger got his first chill and he was stricken with yellow fever. This case showed conclusively that yellow fever had been propagated by the bite of the mosquito, and by no other possible exposure.

The next experiment was to determine whether or not "fomites" could cause yellow fever.

This was done in the following way:

Three large boxes of bedding, consisting of sheets, pillow-slips, blankets, mattress covering, and the like--all of which were contaminated with the discharges of yellow fever patients--were placed in a building of 2800

cubic feet capacity, tightly sealed and battened. Some of the bedding was purposely soiled with black vomit, urine, and faeces. The windows of the building were small to prevent a thorough circulation of air. Wooden shutters prevented the disinfectant action of sunlight. Every entrance--windows and doors--was screened with wire gauze. Dr. Cooke, assisted by two privates, unpacked the boxes and shook the contents vigorously, a procedure designed to disseminate the specific organism throughout the room if it were present. They were then placed on three beds provided and hung around the room in order to bring the men in closer contact with the articles which figured in the experiment. For twenty consecutive nights, the three slept in the uninviting beds. Every morning they packed the filthy--literally speaking--articles back into the boxes and every evening they unpacked them again and distributed them over the three beds. The days were passed in tents in the strictest quarantine. During the twenty days, other bedding, soiled with the filthy, bloody stools of a fatal case, was received in a most offensive stinking condition--but true to the ideal to service to which the men had pledged their lives, they unhesitatingly added them to the rest of the articles. (1) Other non-immunes re-

(1) Dr. Martin--Class Lecture, History of Science
Boston University

peated the experiment for twenty-one days, sleeping in the same garments that had been worn by patients. The result of the exposure of these non-immunes was wholly negative, for not one had the first symptom of yellow fever.

Near that building was constructed another which was built exactly like the first. The room inside was thoroughly ventilated and all the articles in it were as thoroughly disinfected. The room was divided in two by a fine screen. On one side stayed one man, Kissinger's fellow volunteer, John J. Moran, exposed to fifteen mosquitoes: on the other were two other volunteers, not thus exposed. Seven of the mosquitoes immediately settled upon his face and hands and drank their fill of his blood. Soon the other eight tormentors settled upon his almost bare body. Four days later he was stricken with the disease. The two men, living under the same conditions, with the exception of their not being exposed to mosquitoes, remained perfectly healthy.

From this interlocking series of fool-proof demonstrations, Dr. Reed and his associates reached the absolute certainty that <u>yellow fever is always transmitted by infected mosquitoes, and by no other agent</u>.

Thus we see that success, so long elusive, came at the very close of the nineteenth century. "May its cure be wrought out in the early days of the new century!", cried out Major Reed.

We cannot take leave of the study of the history of yellow fever without a great many words of praise for the heroes who figured in the fight. No matter how sincere be our praise, it must necessarily be inadequate. A list of these heroes, together with a few preliminary remarks, constitutes the last section of this thesis; consequently, we leave them for the present.

Carriers

A "carrier", in the case of malaria, is one who has recovered from the disease and has the micro- and macrogametocytes in his blood capable of infecting mosquitoes; or he may be one who has never shown symptoms of the disease and still has the sexual stages in the blood. (1)

Whether or not "carriers" occur in yellow fever has still not been definitely determined. This is due to several causes:

First of all, the enthusiasm and fear which prompted the first studies of the disease necessarily confined the investigations to the causes and controls of the disease.

Secondly, it has been, and in some quarters is still believed that no such factors as "carriers" were significant in the spread of yellow fever.

Thirdly, so little had been known about the organism which causes the disease that it was almost impossible to determine the actuality of "carriers".

However, the presence of "carriers" has sunken into insignificance in view of the gigantic steps and

(1) Matheson, R.--A Handbook of the Mosquitoes of North America--pages 53-55

sweeping success which have characterized the efforts to eradicate the disease.

Today the question is not nearly so important as it was during the latter part of the last century, and we are not seriously concerned with it.

Heredity Transmission

When Dr. Finlay first promulgated the theory that yellow fever was disseminated by mosquitoes, and not by such agents as "fomites", filth, and the like, he raised the question of a transmission of the disease by heredity. This question he himself was unable to answer because of the lack of evidence, and it was left unsettled by the United States Army Commission.

Marchoux and Simond of the French Commission had devoted a great deal of attention to this phase of the problem in their study of yellow fever. They based their conclusions on one apparently positive case which came to their attention and decided that the disease could be transmitted through the egg of an infected Aedes aegypti to the second generation and thence to man. Subsequent work, and particularly that of Philip (1929) has proved irrevocably that such is not the case, and the conclusions of Marchoux and Simond are generally believed invalid. (1)

Once clearly established that yellow fever was transmitted solely by mosquitoes, the question of the species involved and of their characteristics, habits,

(1) Riley and Johannsen--Medical Entomology--
pages 245-258

and geographic distribution, became of vital importance.

Let us first, however, consider the nature of the disease and see wherein lay its cause and danger--factors of such significance that the nations all over the civilized world (particularly the United States and France) willingly spent huge sums of money and time to solve the problem.

Nature of the Disease

To understand completely the nature of yellow fever, we may study it from two points of view:

1. Incubation
2. Symptoms

Our present knowledge of the nature of yellow fever and of its dissemination which has made possible the scientific checking of the disease and will undoubtedly result ultimately in its complete extermination, is, as we have seen, largely the result of the noble and self-sacrificing work of the American Yellow Fever Commission.

Yellow fever was shown by the American Commission to be not a contagious disease, but one which can be transmitted only by the mosquito, Aedes aegypti, or deliberately by injections of blood from an infected person. Normally, the latter method is employed only in experimentation, and may, therefore, be disregarded in any study of the natural cause of the disease.

Early diagnosis of yellow fever is highly desirable. Unfortunately, it is difficult, if not impossible, to make a positive diagnosis of the disease in the early stages, especially in mild cases.

The disease yellow fever has an incubation period of from three to six days. The first symptoms are severe headache and aches in the bones, followed by a sudden fever. The pains are much greater than one would expect from the temperature which is rarely over 103.5°F. In light cases, the temperature is highest on the first day; in moderately severe cases, on the first or second day, when it commences to fall, reaching normal on the fourth, fifth, or sixth day. The headache that accompanies the temperature is sharply severe and is characteristic in that the face is flushed and swollen and the skin dry. There is troubled sleep or insomnia and restlessness. Intense active capillary congestion of the skin and mucous membranes produces yellowing and watery conjunctivae which are more pronounced than that which occurs normally in the tropics. (1)

On the third day comes the state of "calm" during which the temperature is near normal but the pulse very slow. The distress, restlessness, and pain disappear, and the patient is extremely tired--too tired to speak or even move a finger. A significant feature is that the mind remains clear. Passive congestion now takes the place of the active congestion of the first stage. The face is a dusky yellow, the conjunctivae are still

(1) Carrol, F.--Insects and Disease of Man--
page 267

red but dry. They are now distinctly yellow, the gums red and spongy and bleeding spontaneously or on very slight pressure. The stomach is frequently painful, always tender. This may be elicited by pressure over the epigastrium.

In the more severe cases nausea will now return after being absent since the onset of the disease and gastric and intestinal hemorrhages may occur. Jaundice, which was first noticed in the sclerotics may now be general although frequently it does not make its appearance until convalescence.

Albuminuria is generally found on the evening of the third day and if not present by the fourth day, it is rarely found later. It comes on even with very little fever, in an amount out of all proportion to the rise of temperature and increasing in amount with a falling temperature. Albumen making its appearance earlier than the third day is a point indicating an unfavorable prognosis. (1)

A striking but not invariable symptom, and one of ill omen, is the "black vomit," a gushing up through the oesophagus of a coffee-colored or even black fluid, consisting largely of fragments of red blood corpuscles and freed haemoglobin, and sometimes even pure blood.

(1) Carrol, F.--Insects and Disease of Man--
page 268

The period of "calm" may lead to recovery in a few days or there may be a second fever which lasts irregularly for a longer time than the first. (1)

The principal points to be remembered in the symptoms and signs of yellow fever are the early appearance of the albumen, bloody fecies, jaundice, tendency to hemorrhages, tenderness in the epigastrium, lack of correlation between pulse and temperature, and a clear mind, despite delirium.

Considered histologically, the body tissues show a marked change. Reviewing the work of Noguchi, we find that the lungs contain areas of hemorrhage and also small foci of infiltration with polymorphonuclear leucocytes.

The liver is necrotic, and the blood is distributed throughout these necrotic areas, not always being confined in the blood vessels.

The convoluted tubules are dilated with granular excretion and vacuolated cytoplasm. The glomeruli are usually injected, as is the medulla.

Polymorphonuclear leucocytes infiltrate the stomach. The superficial portion of the mucosa is congested.

Because of the enlargement and vesiculation of the nuclei, certain fibres of the heart muscle appear some-

(1) Chandler, A. C.--Animal Parasites and Human Disease--page 71

what swollen.

The spleen contains numerous large phagocytes and follicles atrophied in certain areas.

In the adrenals, there is a marked degree of parenchymatous degeneration, affecting chiefly the medulla.

The pancreas shows that certain of the gland alveoli display small groups of degenerated cells.

As would be expected from the description of the condition of the mind, the nervous system shows nothing abnormal.

Thus we see that yellow fever induces a striking change in the various tissues of the stricken patient.(1)

One may easily understand how yellow fever would be considered, as indeed it was, a fatal disease. It wrought changes of such a pathological nature that comparatively few survived its onset.

(1) Noguchi, H.--Etiology of Yellow Fever--
from the Laboratories of the Rockefeller Institute for Medical Research

Life History

The virulent nature of yellow fever and its great danger of spreading from its endemic centres in Mexico and West Africa, have led to a most exhaustive study of the life history and habits of the infecting mosquito and causative organism.

The yellow fever mosquito (Aedes aegypti L.) (1) formerly known as Stegomyia fasciata, is the invertebrate host of the parasite of yellow fever. The eggs of the adult mosquito are laid on water or in the mud just above the water-line. They do not form rafts, but float about separately. (2) As the eggs can withstand drying for a long time, at least over five months, the filling of receptacles by rain or otherwise assure the young larvae an adequate water supply for their short larval life. The eggs turn black in color (3) and hatch within two days, if the temperature is high. Low temperatures, as in the winter months, prolongs the hatching until the temperature becomes high again. The larval life, once the eggs have hatched, is comparatively short, occupying six to ten days, if the temperature is fairly high. Once again, cool weather prolongs devel-

(1) Fernald, H. T.--Applied Entomology--page 309
(2) Bolduan--Public Health and Hygiene--pages 135-138
(3) Ibid

opment. The mature larvae are robust, rather stout, with a relatively short, somewhat pointed siphon, which bears a pair of small hair-tufts just beyond the pecten. The scales of the comb are distinctive--sole-shaped with a long, curving apical spine and several sub-apical spines. Great activity is noticed in the larvae. They are particularly responsive to disturbances of any kind, darting to the bottom of the water at the slightest disturbance, or even at a passing shadow. On account of this habit, their presence is often difficult to detect unless the inspector can take time, he himself remaining very quiet, to observe them return noiselessly to the surface. Even then they may be overlooked as the larvae press themselves close to the bottom and are not easily dislodged. This ability to burrow themselves frequently enables them to breed continuously in containers of drinking waters which are intermittently emptied and refilled, since many of them escape being dislodged. (1) They are not resistant to drying and die in a few hours in a dry place, though capable of living nearly two weeks on moist ground.

The pupal stage is comparatively short. Under normal conditions the pupae transform in a day and a half or two days. The entire cycle from egg to adult

(1) Matheson, R.--Medical Entomology--page 223

seldom takes place in less than nine or ten days, and probably twelve to fifteen days is more usual under ordinary conditions. Unfavorable conditions may easily prolong the period of development several months. (1) Within its permanent range, the mosquito breeds throughout the year; generation succeeds generation with great rapidity when water, the necessary warmth, and a blood supply are available. During the colder months of the year, the reproductive process is slowed down. At the same time the eggs or larvae remain dormant.

Male mosquitoes will now ordinarily live for fifty days, but the females frequently live several times as long a period of time. Strange as it appears at first, the length of life is shortest under the most favorable conditions: namely, plenty of blood for food and plenty of moisture and suitable places for egg-laying.

Once the female mosquito has become infected, it remains infective for the remainder of its life. The male, if it alights upon the body of a human being, will not suck any blood and soon flies away without having done any injury at all.

The breeding places are of the utmost importance in the study of the control of yellow fever, but it may be mentioned that Aedes aegypti breeds in cisterns,

(1) Chandler, A. C.--Animal Parasites and Human Disease page 447

water barrels, pitchers, and the various water receptacles about the house. They will not breed in muddy water although it has been shown that the larvae will thrive in brackish water. (1)

Although the yellow fever mosquitoes will long be known under the specific name of Stegomyia fasciata Fabr. the species is apparently correctly designated as Aedes aegypti Linn., having stood for several years under the name of Aedes calopus Meig. (2) The adult mosquito is beautifully marked with silvery white or yellowish white bands and stripes on a nearly black background, which has earned for it the name "tiger mosquito." It has a "lyre-like" pattern dorsally on its thorax, i.e., two outer curved yellowish white lines and two median parallel lines. The legs are commonly conspicuously banded and the last joint of the hind leg is entirely white. The head is covered with broad flat scales with only a single row of upright forked scales. (3) The wings are clear and somewhat iridescent. The female measures 3.3 to 5 mm.; the male, 3 to 4.5 mm.

Aedes aegypti is preeminently a domestic species, being found almost exclusively about the habitations of man. Its long association with man is shown by many of its habits. It approaches stealthily from behind, re-

(1) Chandler, A. C.--Animal Parasites and Human Disease page 447
(2) Herms, W. B.--Medical and Vertimerary Entomology--page 127
(3) Ibid

treating upon the slightest alarm. When one is sitting at a table or desk, the ankles and the underside of the hands and wrists are favorable points of attack. (1) Unlike other mosquitoes who have a piping or humming sound when attacking, Aedes aegypti suppresses the "song" so that its bite comes silently and without warning. It hides wherever it can, concealing itself in garments, working into pockets and under the lapels of coats, and crawling up under the clothes to bite the legs: in houses it will hide in dark corners, under moldings, behind the heads of old-fashioned bedsteads, under chairs, behind pictures, etc.; the wariness of its larvae:--all these are the results of lessons learned from long and close association with man. (2) Owing to its ability to "stow away" the yellow fever mosquito has been, and annually is, widely distributed over the world. (3)

The search for the causal organism of yellow fever has been carried on most assiduously for many years, and discoveries have been announced from time to time. Thus Sanarelli in 1897 declared the organism to be Bacillus icteroides (as has been suggested on page 12). Seidelin in 1909 described Paraplasma flavigenum (belonging to the protozoan family Babesiidae) as the causal agent.

(1) Riley and Johannsen--Medical Entomology--pages 245-258
(2) Chandler, A. C.--Animal Parasites and Man--page 444
(3) Ibid

Folsom records the presentation of the theory that "a protozoan parasite, the sexual cycle of which, ending in the development of sporozoites, has been traced in the body of Stegomyia." (1) This causative organism was supposedly a coccidium, but subsequent work has definitely invalidated this conclusion. In 1919 Noguchi advanced most conclusive evidence that the causative organism of yellow fever is Leptospira icteroides. (2)

It has been known for a long time that spirochaetes are unquestionably responsible for such diseases as relapsing fever, syphilis, infectious jaundice, as well as being associated with other organisms to cause sores or ulcers.

In general, the diseases caused by spirochaetes may be divided into four groups. First, there is the type in which the spirochaetes live and multiply mainly in the blood. The various forms of relapsing fever belong to this group. Second, there is the type being characterized by spirochaetes making a general invasion of the body and living in its tissues. To this type belongs syphilis. Third, there are infections and lesions which may or may not be caused by an association with other organisms. To this type belong ulcers and spirochaetal bronchitis. Fourth, and most important in

(1) Folsom, J. W.--Entomology--page 305
(2) Herms, W. B.--Medical and Vertinerary Entomology--page 152

our study of yellow fever, there are the Leptospira diseases in which spirochaetes of the genus Leptospira invade the body and localize primarily in the liver and kidneys. To this belong infectious jaundice and Japanese seven-day fever. (1)

Whatever the infective agent may be, it is capable of passing through a Berkefeld filter and thus belongs to the puzzling group of "filterable viruses."

The virus is believed to be present in the circulation only during the first three days of the disease; blood in the infective stage quickly loses its virulence on exposure to air and becomes non-virulent at a temperature of 55° C. within five minutes. (2) Added to that, the virus cannot develop within the body of the mosquito at a temperature below 21° C. to 20° C.

Noguchi, (1919) in a series of papers, presented apparently definite evidence that the disease was due to a spirochaete which he named Leptospira icteroides, but his work met with much criticism, and he himself, before his tragic death due to yellow fever in West Africa, came to recognize that he had probably been dealing with a mixed infection or an incorrectly diagnosed case of infectious jaundice and its organism Leptospira icterohaemorrhagie. (3)

(1) Chandler, A. C.--Introduction to Human Parasitology page 49
(2) Herms, W. B.--Medical and Vertinerary Entomology--page 152
(3) Riley and Johannsen-Medical Entomology-pages 245-258

Today the question is still not definitely determined. The scientific world is more prone to accept Noguchi's organism because of the vast amount of careful work which he did in his experimentations. The gradual eradication of the disease has tended to lessen the efforts to isolate the causative organism. But there is no question that the solving of the mystery of the mosquito role and the partial solving of the causative organism role have vied in exceedingly vital significance in the control of yellow fever.

We have seen how the development of the mosquito is seriously hampered and slowed down in unfavorable temperature. In parallel manner, we have observed that the virus cannot develop under the same circumstance. The extreme sensitiveness to heat and cold of both the mosquito carrier and the causal agent explains, to a large degree, the restricted geographical distribution of the disease for which they are responsible.

Distribution of Yellow Fever

The study of the distribution of the yellow fever mosquito is obviously important in any intendedly fairly complete study of the history and control of the disease. It is only by observing its place of origin and spread into subsequent endemic and epidemic centres that we may gain a full notion of the importance of the disease, for in having accurate knowledge as to its distribution, we may prepare for or know of its occurence. The procedures of control are but a step away.

Generally speaking, we may say that yellow fever occurs in the tropics throughout both hemispheres and, during warm weather, may extend to the temperate regions but can survive there only while the temperature is fairly high. (1) Or we may say that the mosquito is distributed from 40 degrees north latitude to 40 degrees south latitude, in a belt extending around the world.

Aedes aegypti has very wide distribution since, being a domestic mosquito, having a fairly long life in the adult stage, and having the ability of hiding itself in the most ingenious ways, it is particularly subject to carriage for long distances on board vessels, in

(1) Fernald, H. T. -- Applied Entomology -- page 309

railway trains, even packed in baggage.

The endemic centres of yellow fever are found in tropical America, Mexico, Brazil, Ecuador, Salvador, and on the west coast of Africa. If once introduced, the disease may become epidemic in any country where the insect host is present. Yellow fever has made its appearance a number of times in the United States and, before the discovery of the methods of transmission, created panics from time to time, especially in communities bordering on the Gulf of Mexico. Its last appearance in this country -- and it will undoubtedly remain the last -- was in New Orleans in 1905.

During the building of the Panama Canal, the various health authorities feared that with the completion of the canal would come an increased possibility of the introduction of the disease into places where it had until that time been unknown. The result with a non-immune population would have been appalling. Fortunately, the famous fight waged against the disease in the Canal Zone has eliminated this menace.

On the other hand, there are places in this country wholly outside the normal range of Aedes aegypti where the disease has raged. Such are New York, Boston, and Philadelphia, which have suffered fearful and notable

epidemics. These outbreaks have been due to the introduction of infected mosquitoes during the heat of summer when they have not only conveyed the disease in all its power but have found conditions favorable for their multiplication. Or, uninfected mosquitoes have been brought in accidentally and developed in large numbers. All that is needed to start a severe epidemic in that case is to have them accidentally introduced to a few cases of the disease.

Yellow fever has failed, during all the past centuries, to gain access to the Far East only because of the long sea journey which exceeds the incubation period of the disease, and makes it possible to discover cases of yellow fever and block them, or mosquitoes which might have fed on them, from entering. Today, however, the danger is greater. Sometimes altered environmental conditions cause some diseases to disappear and others to come. But fortunately, the disease of yellow fever has so far never been introduced into the Far East and it is to be hoped that it will never gain access to that portion of the world at all.

Thus we see that yellow fever is, for the most part, endemic in certain regions but may spread epidemically to others. The distribution of the disease serves

as a warning and offers the opportunity of drawing up preventive measures. Having discussed the history of yellow fever, including the highly interesting and instructive experiments surrounding it, as well as the Nature of the disease, its life history and distribution, it may now be expedient to record the various methods and procedures of control which have been used and are still being employed in the control of the disease.

The Control of Yellow Fever

There seems to be little natural immunity to yellow fever. One attack confers immunity and second attacks are very rare. It is less fatal in the younger age groups (probably because of a normal, higher resistance than in older age groups) and in the negro race, which possesses a certain degree of racial immunity. At least they have the disease in milder form than whites, Indians, or Chinese.

Until the discovery of the organism causing yellow fever by Noguchi and its isolation in pure culture, the treatment of yellow fever consisted only of careful nursing and in the maintenance of the best hygienic conditions. There are no drugs known which have any value as specifics against the disease. Recently, however, Noguchi and his fellow workers at the Rockefeller Institute have demonstrated the development of antibodies in animals and man inoculated with dead cultures of the leptospira, and from the results of vaccination in guinea pigs, concluded that with the inoculation of a sufficient quantity of dead organisms they were rendered immune to subsequent infection. Encouraging results have

been obtained from the vaccination of human beings. Of 8000 non-immune persons vaccinated in tropical America, excluding those exposed to the disease just before and immediately after vaccination, no cases of yellow fever have developed, while among unvaccinated persons during the same period and in the same locality, there have been about 700 cases of the disease. (1)

A therapeutic serum has also been prepared for treatment of yellow fever. According to Noguchi, persons treated with a sufficient quantity of the serum before the third day have invariably recovered. By the fourth day of illness, the organs have become so injured and degenerated that they are irreparable.

Despite these encouraging figures, there is no doubt that the vaccination and serum in the treatment of yellow fever are still in an experimental stage. The entire world is firm in the trust and hope, heightened by the reduction of the usual 50 to 60 per cent mortality from yellow fever to 9 per cent by the use of the serum, that medical science will do its part in the divorcing of yellow fever from the face of the earth.(2)

But these measures are but recent discoveries and innovations which have come in with the development of physiological serums and vaccinations. In studying the

(1) Chandler, A. C.--Animal Parasites and Human Disease--page 272

(2) Ibid

control of yellow fever, we are more likely to observe the physical means--not because of any desire to minimize the advantages and benefits of the medical treatments proper--but rather because the eradication of the disease consists in the application of sanitary measures to exterminate the causal organism, as a matter of fact. In the face of an epidemic, this procedure can now be supplemented by vaccination to cut off the supply of non-immunes from infected mosquitoes. The value of immunization as an emergency measure does not diminish the importance of anti-mosquito campaigns, since the elimination of both factors--non-immune human beings and infected mosquitoes--is necessary for the complete eradication of yellow fever. (1)

As stated before, the subject of yellow fever is a matter of historical interest only--but the various means of control of the disease are still of the utmost importance. Negligence of the slightest sort might result in an epidemic which would amount to a loss of numberless lives and tremendous sums of money.

There are two important facts to be kept in mind; first, that without the yellow fever mosquito yellow fever cannot spread even though a case is introduced into a community; second, that the yellow fever mosquito

cannot become infected unless it has bitten a diseased patient some time during the first three--or four, in some cases--days of the illness. These factors cannot be too greatly stressed--for upon them depends the entire subject, with all its ramifications, of the control of the disease. (1)

Of first degree in importance in the prevention and control of yellow fever is the early recognition of the disease. To be on the safe side during an epidemic or threatened epidemic, every case of yellow fever should be immediately reported to the proper authorities since immediate, dependable attention is essential.

The house in which yellow fever occurs should be placarded in order that any non-immunes who are in its vicinity may not be unnecessarily exposed to an Aedes mosquito which could very easily have just become infective from a meal of the diseased blood of the patient. The process of placarding a house takes but a few moments and should be faithfully carried out with every newly discovered case of the disease.

The purpose of placarding vies with that of isolation. A patient of the disease should be isolated with particular reference to screening. Isolating the diseased person for an expedient period of time may do away

(1) Fox, C.--Insects and Disease of Man--
page 268

with the possible danger of his being a "carrier." It is obvious that a perfectly isolated case of yellow fever must, by the very definition, be absolutely incapable of spreading the disease through even the most remote chance.

In a series of very informal but instructive lectures delivered at the United States Public Health Service School of Instruction by H. R. Carter, Senior Surgeon of the United States Public Health Service,(1) the subject of prevention and control was discussed.

"In artificial containers," stated Dr. Carter, "there are three methods you may adopt to get rid of mosquito larvae or eggs: Turn the water out; screen the container; or, if these two are impracticable or not permissible, oil the container.....In turning the water out of the container, turn it completely out; do not leave any water in it, or you will have to do your work over again. This mosquito has been turned out of water jars for generations. Those that have been turned out have not bred any progeny, and only the progeny of those that knew how to take care of themselves are alive. Thus the instinct to save themselves is strong in them now, and I must say that a great many of them seem to know how to take care of themselves. For example, of 100

(1) Supplement #19 to the Public Health Reports, United States Public Health Service

larvae in a jar that has been turned out, if you leave 50 drops of water in the jar, you will find 99 of the original larvae in the bottom.....get rid of every drop of water that is in it."

I have recorded this excerpt to give some suggestion as to the infinite care which must be exercised. Such care will more than be worth while in the lowering of the mortality from this disease. And certainly past experience has proved that any amount of precaution and care is worth the price entailed.

E. M. Woodworth, Surgeon-General of the United States Marine Hospital Service, in 1878 justly believed quarantine important in the control of yellow fever. Unfortunately, he did not realize that mosquitoes were at all instrumental in the conveying of the disease. In a letter which he addressed to the medical officers of the Marine-Hospital Service, he comments upon the fact that attendants, burning the "effects" of dead yellow fever patients never contracted the disease. But today the observance of Quarantine is one of the most vital factors which can be practised in the conquest against yellow fever.

The Aedes aegypti has, as has been stated, the ability to "stow away" on sea vessels and trains. Sub-

sequently, the danger of introducing the mosquito into other ports, especially if the temperature is warm, is obvious. Hence, in recent years, ships and railroad trains which enter a port or centre within the distribution areas of the mosquito are very minutely and rigidly inspected. Fumigation is liberally carried out and small chance indeed has an Aedes mosquito which has traveled aboard in hiding, after one of these inspections has taken place.

As a matter of fact, disinfection is not required. Fumigation to kill mosquitoes should be practised in a screened room to which the patient should be transferred, after which the rest of the house, including the room previously occupied by the patient should be fumigated.

Disinfection is useless if employed for the purpose of killing any supposed "germs"--for we have seen how the United States Army Commission proved quite conclusively that "fomites" and "germs" are not at all causal in the dissemination of yellow fever.

Parenthetically, however, fumigation will, at the same time, kill many other injurious and harmful organisms.

Screening constitutes one of the best modes of control that is known. Most importantly, it is highly

effective. Added to that, it is comparatively easy to use. Where economy is a matter to be seriously considered, screening is a welcome means of control--for it is relatively cheap.

An entire community, of course, would find it impracticable. But as a protection to himself and family, each householder should screen his individual house against mosquitoes.

There are a few facts about screening which, though simple, are usually too easily overlooked. To insure maximum protection against mosquitoes, the following facts should be religiously observed:

1. The netting used should have meshes fine enough to prevent the passage of mosquitoes (at least 18-20 meshes to the inch).

2. It is important to screen the windows and doors of the house. It is doubly important to screen the beds of fever patients.

3. Mosquitoes can bite through mosquito nets when any part of the patient's body is in contact with the netting.

4. Frequent examinations should be made to see that there are no torn places in the netting or that no mosquitoes have found a lodgment inside.

5. The netting should be well tucked in to keep mosquitoes from entering.

6. If mosquitoes are found within the netting they should be killed inside and not merely driven or shaken out.

7. All cases of fever should be promptly reported to the local health officer. Awaiting his arrival they should be covered with a mosquito bar. (1)

The International Health Board has been very successful in the use of fish for the extermination of larvae of the Aedes aegypti in Nicaragua, Peru, and Eduador. The fish are placed in wells, cisterns, rain barrels, water bottles--in fact in all but the smallest water containers. In Peru a fish known locally as Chalaco has been found to be the most useful. In Nicaragua, the Poecilia sphenops has been successfully used, which is probably the same fish as the one used successfully in Peru. Other fishes used in Peru are known locally as Life, Majarra (Aequidens rivulatus), Cachuelo, Trinon, and Bagre (a small cat fish). (2)

A campaign of education should be carried on so that people would understand what is being done for their good, and what they should do to help out the situation. It is only with the cooperation of everybody

(1) Treasury Department, Bureau of P. H. and M. H. S.--How to Prevent Yellow Fever--Washington, July 31,'05
(2) Fox, C.--Insects and Disease of Man--page 270

concerned that the best results are obtained. So far as general measures are concerned, the work of eradicating yellow fever mosquitoes must be carried on energetically by an organized corps, consisting of laborers working under the supervision of inspectors. The city should be divided into districts, and a sufficient number of laborers and inspectors assigned to work therein, so that the territories can be covered once a week. Their duties are to hunt out all places in which yellow fever mosquitoes are breeding and do away with them by spilling, filling, oiling, screening, or any other method which has been discussed. (1)

From time to time the United States Public Health Service has issued short, comprehensive, instructive lectures through the medium of the radio. Listeners all over the world are informed of the nature, distribution, dangers, and other facts of interest concerning a designated disease. Yellow fever was the subject of one such broadcast. It is obvious how much benefit may be derived from such a source of education in stamping out the disease. (2)

Summing up the points we have discussed as well as adding several new ones we may review these facts which bear on mosquito destruction: namely, the facts which

(1) Fox, C.--Insects and Disease of Man--page 269
(2) Public Health Broadcast, No. 283

are important in the control of yellow fever:

1. Mosquitoes live in the vicinity in which they breed.

2. Mosquitoes breed only in water (not cesspool water), the wriggler being able to live in the water from seven to twelve days. It must come frequently to the surface to breathe, a procedure which is prevented by pouring coal oil on the surface of the water.

3. Destruction of the breeding places means the destruction of the mosquitoes.

4. Fine wire netting placed over cisterns, wells, and tanks of water in everyday use will prevent the mosquitoes from gaining access to a potential breeding place.

5. Goldfish or minnows and certain fish in Peru will devour the mosquito wrigglers.

6. Fumigation has proved to be very effective in the destruction of mosquitoes.

7. Success in mosquito destruction depends upon the cooperation of the members of the entire community.

8. While the infection of yellow fever is carried by a single species of mosquito, to insure its destruction, it is necessary to destroy all mosquitoes.(1

(1) Wyman, Walter--Surgeon General, --Facts Bearing on Mosquito Control--Washington, July 31, 1905

Dr. Rucker, Assisstant Surgeon General of the United States Public Health Service, has compiled an extremely interesting and educational booklet on "The Administration of a Yellow Fever Campaign." Since we are about to leave the subject of control, it may be well to show how such an administration would be organized.

The objects of the campaign would necessarily be:

1. Prevention of the breeding of Aedes aegypti.

2. Locating all persons sick of yellow fever or any suspicious fever as early as possible in the disease.

3. Preventing of the mosquito from biting those sick people and becoming infected.

4. Destruction of all infected mosquitoes.

A commanding officer is in charge of and responsible for the administration of the entire campaign. To expedite matters the work may be divided among several senior officers.

Under the direction of the commanding officer is the executive officer who conducts all the branches of the executive division of the work. The commanding officer also directs the field force which is made up of

men appointed as inspectors and investigators.

An arrangement is made with the local boards to insure the maximum amount of mutual understanding and cooperation.

There is a force of men whose duty it is to take care of the division of disbursements and the department of statistics.

A trained corps of doctors, nurses, and attendants are important for the work in preparing and directing the detention camps, isolation hospitals and wards.

Then, of course, would come the actual work in the prevention of the disease by the various methods discussed. (1)

The control of yellow fever, as it has been accomplished by the various countries subjected to the disease, is something of which the governments may well be proud. From a panic-stricken, futile series of attempts to eradicate the disease came a cool, logical reasoning which could not help but solve the mystery.

Many factors have been instrumental in effacing the disease, and it is with the hope that the various measures of control will in time erase yellow fever completely that we are forced to admit that it may spread again into regions where it has apparently been

(1) Supplement No. 15 to the Public Health Reports June 12, 1914

eliminated.

With the development of aeroplane transportation, the most distant parts of the Americas are brought close to our doors. The introduction of a single incipient case or "carrier" (?) of yellow fever might be sufficient to start a small focus from which the disease could spread with great rapidity. Realizing the possibilities we must not become lax in our efforts. With the aid of medical science and past experience, we may feel sure that yellow fever will never become a serious menace again.

Conclusions and Summary

The year after the United States Army Commission had completed its classical experiments in Cuba it expressed its conclusions in eleven postulates as follows:

1. The mosquito, Culex fasciatus, serves as the intermediate host for the parasite of yellow fever.

2. Yellow fever is transmitted to the non-immune individual by the bite of the mosquito that has previously fed on the blood of those sick with this disease.

3. An interval of about 13 days or more after contamination appears to be necessary before the mosquito is capable of conveying the infection.

4. The bite of the mosquito at an earlier period after contamination does not appear to confer any immunity against a subsequent attack.

5. Yellow fever can also be experimentally produced by subcutaneous injection of blood taken from the general circulation during the first and second days of the disease.

6. An attack of yellow fever produced by the bite of the mosquito confers immunity against the sub-

sequent injection of the blood of an individual suffering from the non-experimental form of this disease.

7. The period of incubation in 13 cases of experimental yellow fever has varied from 41 hours to 5 days and 17 hours.

8. Yellow fever is not conveyed by fomites, and hence disinfection of articles of clothing, bedding, or merchandise, supposedly contaminated by contact with those sick of this disease, is unnecessary.

9. A house may be said to be infected with yellow fever only when there are present within its walls mosquitoes capable of conveying the parasite of this disease.

10. The spread of yellow fever can be most effectually controlled by measures directed to the destruction of mosquitoes and the protection of the sick against the bites of these insects.

11. While the mode of propagation of yellow fever has now been definitely determined, the specific cause of this disease remains to be discovered. (1) (Noguchi's Leptospira icteroides may be the answer to the question of the identity of the specific cause.)

These conclusions sum up the results of the splendid work accomplished by the members of the Commission. No

(1) Herms, W. B.--Medical and Vertinerary Entomology--page 152

story in all the history of scientific achievement seems to make stronger appeal to people than this dramatic tale of the conquest of yellow fever. Certainly the circumstances surrounding it have justified such an appeal. These circumstances may be noticed in a summary:

Yellow fever, one of the great scourges known to man, first appeared in Central America over three hundred years ago. From there it spread epidemically into the Gulf of Mexico; thence into Charleston, Mobile, New Orleans, Galveston, and northwards even into New York and Boston. The disease is much more virulent in the tropics than in the north, because the colder temperatures are unfavorable to the growth of the causal mosquito.

It was not until the United States Army Commission, consisting of Major James Carroll, Dr. Jesse W. Lazear, and Dr. Aristides Agramonte, under the direction of Dr. Walter Reed, that the theory of yellow fever as a mosquito-borne disease was definitely proved.

The experiments of the Commission showed conclusively that fomites had nothing to do with the disease. Several of the army corps, as well as members of the Commission, bravely underwent human experimentation in the attempts to solve the secret of yellow fever.

Whether or not "carriers" occur in yellow fever has still not been definitely determined.

The French Commission had devoted a great deal of attention to the aspect of heredity transmission with the conclusion that yellow fever may be transmitted through the egg of an infected mosquito to the second generation and thence to man. Philip (1929) has proved irrevocably that such is not the case. His experimentations have invalidated the theory of heredity transmission.

Yellow fever has an incubation period of from three to six days. The characteristics of the disease are singular. The principal points to be remembered in the symptoms and signs of yellow fever are the early appearance of the albumen, bloody faeces, jaundice tendency to hemorrhages, tenderness in the epigastrium, lack of correlation between pulse and temperature, and a clear mind, despite delirium. The disease has also a marked change in the various tissues histologically.

The entire life cycle from egg to adult seldom takes place in less than nine or ten days, and probably twelve to fifteen days is more usual under ordinary conditions.

Once the female mosquito has become infected it re-

mains infective for the rest of its life.

It is not definitely known today what the causative organism is. Leptospira icteroides was presented by Noguchi (1919) as the causal organism, but the conclusion has been questioned.

Generally speaking, we may say that yellow fever occurs in the tropics throughout both hemispheres and, during warm weather, may extend to the temperate region but can survive there only while the temperature is fairly high.

Several therapeutic sera have been prepared for the treatment of yellow fever, but these sera and vaccinations are still in an experimental state. The best methods of control known are placarding, isolation, fumigation, screening, and the use of fish.

In the organization of an administration of a yellow fever campaign there are certain standard divisions of departments and labor which would set about to cope with the disease.

It is hoped and believed that the knowledge now available concerning yellow fever is of such a nature that it will never become a menace to any part of the world.

Roll of Honor

Participants in Yellow Fever Investigations in Cuba

Major Reed, when he sent his report to Washington officials, said of the offer of Kissinger and Moran, "In my opinion, this exhibition of moral courage has never been surpassed in the annals of the Army of the United States."

The world says the same thing of all the participants in the yellow fever investigations in Cuba.

The Secretary of War, Hon. Elihu Root, in his annual report, 1902, said with reference to the conquest of yellow fever in Cuba in 1900-1901:

"The brilliant character of this scientific achievement, its inestimable value to mankind, the saving of thousands of lives, and the deliverance of the Atlantic seacoast from constant apprehension, demand special recognition from the Government of the United States."

The Congress has, in concurrence with his opinion, by an act approved February 28, 1929, authorized and directed the Secretary of War to publish annually in the Army Register a Roll of Honor on which shall be carried the following names, and to define in appropriate lang-

uage the part taken by each of these persons in the yellow fever investigation in Cuba. The same act provided that a gold medal be presented to each person named in the roll, or to the representatives of those who have died.

ROLL OF HONOR

The Yellow Fever Board.

1. Major Walter Reed, Chairman. Died of Appendicitis Nov. 23, 1902.

2. Major James Carroll. Had experimental yellow fever. Recovered, but died of heart disease Sept. 16, 1907.

3. Dr. Jesse W. Lazear. Died Sept. 25, 1900 of yellow fever, not experimental, in Camp Columbia, Cuba.

4. Dr. Aristides Agramonte. Now professor in the Medical School of the University of Havana.

Persons subjected to yellow fever experiments.

1. Private John H. Andrus, Hospital Corps.

2. Mr. John R. Bullard. Civilian. Graduate of Harvard.

3. Private A. W. Covington. 23 Battalion, C.A.C.

4. Private William H. Dean. Troop B, 7 Cavalry.

5. Private Wallace Forbes. Hospital Corps.

6. Private Levi E. Folk. Hospital Corps. Yellow fever and fomites.

7. Private P. Hamann. 23 Battalion, C.A.C.

8. Private James F. Hanberry. Hospital Corps. Yellow fever and fomites.

9. Private Warren G. Jernegan. Hospital Corps. Yellow fever and fomites.

10. Private John R. Kissonger. Hospital Corps.

11. Mr. John J. Moran. Civilian Clerk.

12. Private William Olson. Hospital Corps.

13. Private Charles G. Sontag. Hospital Corps.

14. Private Clyde L. West. Hospital Corps.

Exposed to fomites only.

1. Dr. R. P. Cooke.

2. Private Thomas M. England. Hospital Corps.

3. Private James Hildebrand. Hospital Corps.

4. Private Edward Weatherwalks. Hospital Corps.

THE HISTORY AND CONTROL OF YELLOW FEVER

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Deaths in Havana from Yellow Fever during Years
1893 to 1902 Inclusive

	1893	1894	1895	1896	1897	1898	1899	1900	1901	1902
January	15	7	15	10	69	7	1	8	7	0
February	6	4	4	7	24	1	0	9	5	0
March	4	2	2	3	30	2	1	4	1	0
April	8	4	6	14	71	1	2	0	0	0
May	23	16	10	27	88	4	0	2	0	0
June	69	31	16	46	174	3	1	0	0	0
July	118	77	88	116	168	16	2	30	1	0
August	100	73	120	262	102	16	13	49	2	0
September	68	76	135	166	56	34	18	52	2	0
October	46	40	102	240	42	26	25	74	0	0
November	28	23	35	244	26	13	18	54	0	0
December	11	29	20	147	8	13	22	20	0	0

(1)

This chart shows the result of control based upon the work of the American Yellow Fever Commission. Surely it is eloquent in its praise of their splendid work.

(1) Doane, R. W.--Insects and Disease

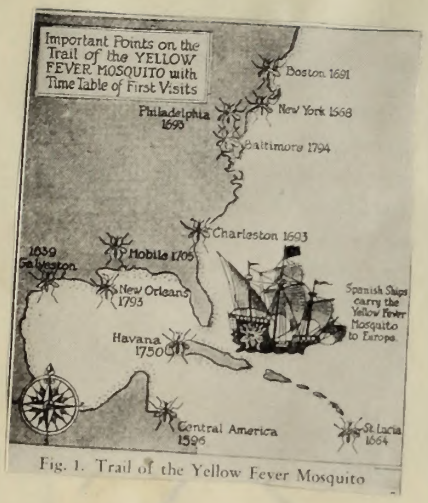
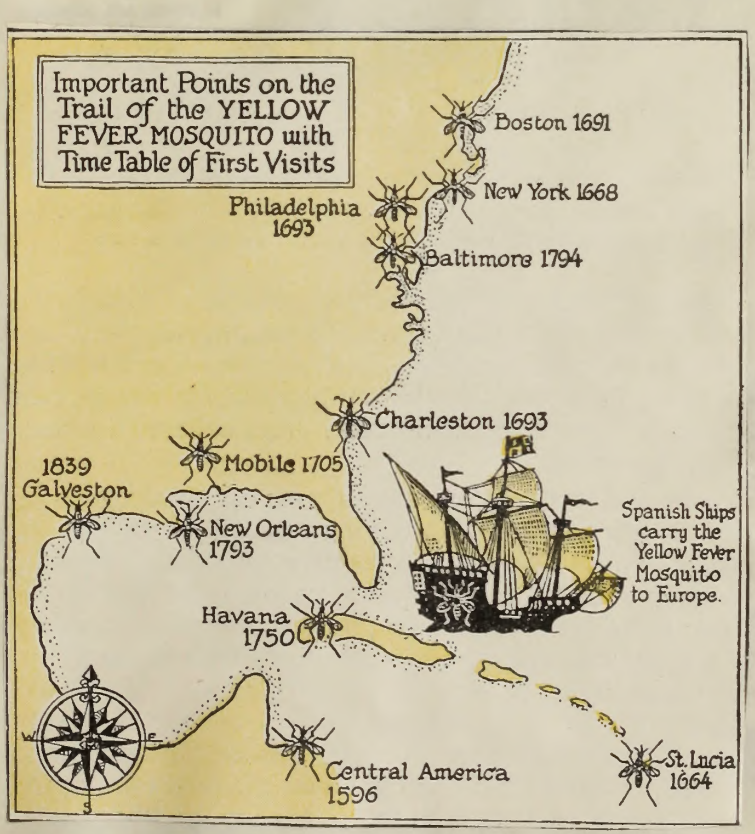
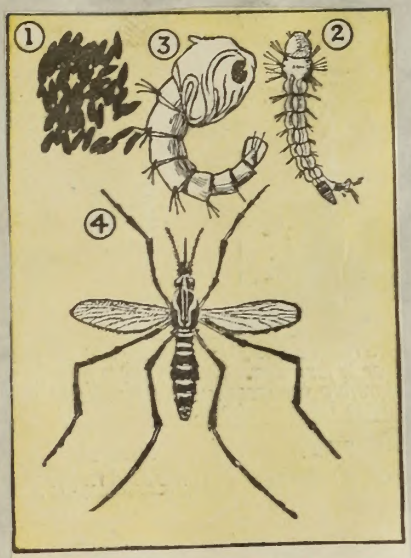


Fig. 1. Trail of the Yellow Fever Mosquito

The Distribution of yellow fever





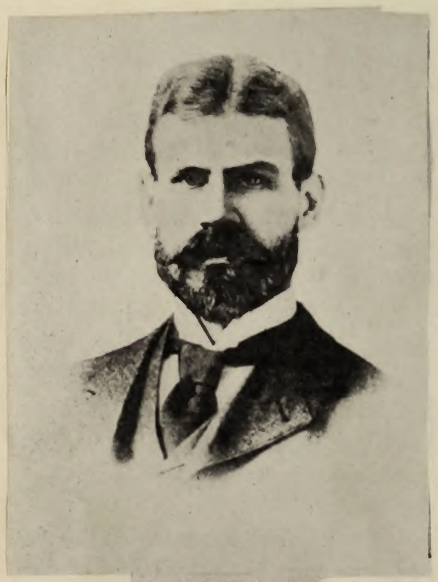
Stages in life of yellow fever mosquito: (1) Eggs deposited in a close-lying mass (enlarged) (2) Full-grown "wiggler" (enlarged) (3) Pupa (enlarged) (4) Female adult mosquito, the carrier of yellow fever (enlarged)

The Yellow Fever Mosquito. The figure at the left is a male Mosquito which is harmless. The two figures at the right show the female.

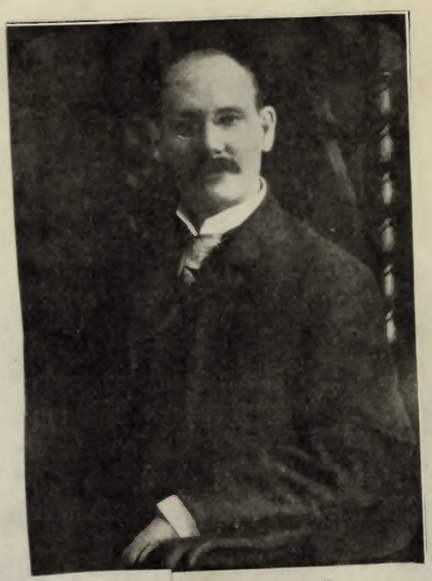

SIDE A
SIDE B

Major Walter Reed

Dr. Aristides Agramonte

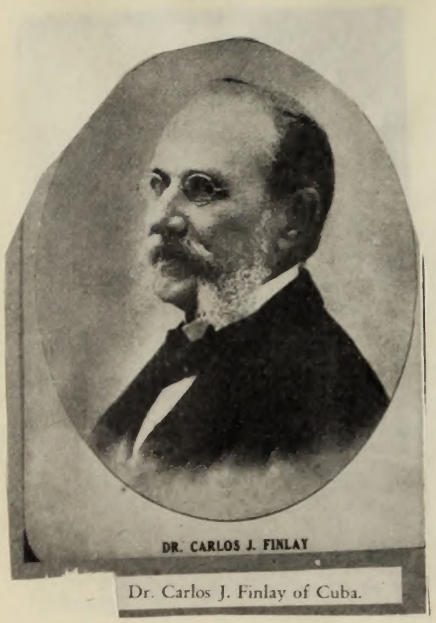


Dr. Jesse W. Lazear.



Dr. James Carroll.

The Members of the United States Army Commission

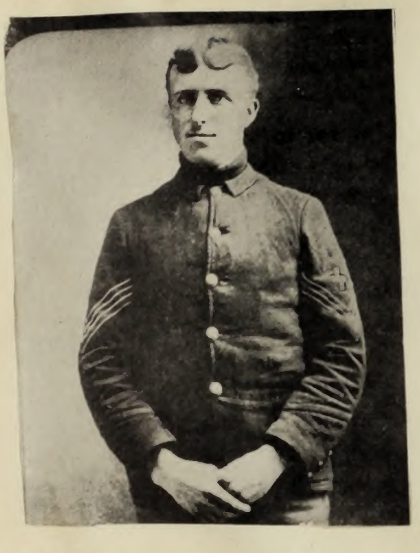


Dr. Carlos J. Finlay of Cuba.

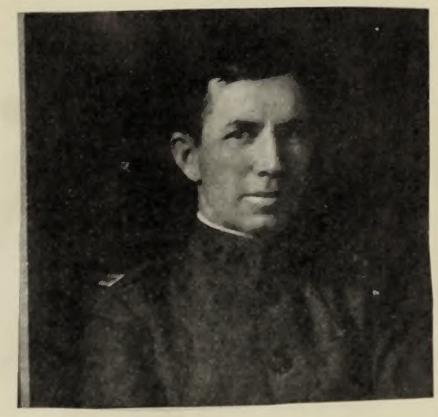
One of the first men to suggest that yellow fever is carried by a mosquito.

Dr. Hedeyo Noguchi in his laboratory.

Discoverer of Leptospira icteroides as the causal organism of yellow fever.



Private John R.
Kissinger



Private John J. Moran

Camp Lazear--the "infected clothing building." Dr. Carroll is standing beside it.